IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

THERMO FINNIGAN LLC, Plaintiff-Counterclaim Defendant, v. APPLERA CORPORATION, Defendant-Counterclaim Plaintiff.	Civil Action No.: 04-1505-GMS

THERMO'S OPENING MARKMAN BRIEF

OF COUNSEL:

William F. Lee
Wayne L. Stoner
Richard Goldenberg
Stephen M. Muller
Mary Rose Scozzafava
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
(617) 526-6000

Dated: January 20, 2006

Frederick L. Cottrell, III (#2555)
(Cottrell@RLF.com)
Kelly E. Farnan (#4395)
(Farnan@RLF.com)
Richards, Layton & Finger
One Rodney Square
920 N. King Street
P.O. Box 551
Wilmington, DE 19899

(302) 651-7700

Attorneys for Thermo Finnigan LLC

TABLE OF CONTENTS

Introduction 1

I. Technological Background 1

A. Introduction to Capillary Electrophoresis 1

1. Electric Fields, Ions, and Ion Movement 1

2. Ion Movement in a Capillary 2

3. Ion Detection US1DOCS-5436350v5

B. Electroosmotic Flow 7

C. Effect of Temperature on Separation 8

II. The '654 Patent 8

A. The Invention 8

B. The Prosecution History 10

III. Basic Principles of Claim Construction 11

IV. Disputed Claim Terms for the '654 Patent 12

A. "Anions" 12

B. "Capillary Electrophoresis" 16

C. "Carrier Electrolyte" 18

D. "Target Temperature" 19

E. "Detecting Said Anions by Simultaneously Monitoring Said Sample at Two Different Wavelengths" 21

F. "Maintaining the Temperature in Said Capillary to Within ±0.5° C. of Said Target Temperature" 25

G. "Electroosmotic Flow" 28

H. "Electroosmotic Flow Modifier" 29

Conclusion 31

TABLE OF AUTHORITIES

Cases

Interactive Gift Express, Inc. v. Compuserve, Inc.,
256 F.3d 1323 (Fed. Cir. 2001) 14 20

Masimo Corp. v. Mallinckrodt Inc.,
18 Fed. Appx. 852, 855 (Fed. Cir. 2001) 18

Phillips v. AWH Corp.,
415 F.3d 1303 (Fed. Cir. 2005) ..... *passim*

Schwarz Pharma, Inc. v. Warner-Lambert, Co.,
95 Fed. Appx. 994, 996, 998 (Fed. Cir. 2004) 17

Vitronics Corp. v. Conceptronic, Inc.,
90 F.3d 1576 (Fed. Cir. 1996) 15, 26

Statutes and Other Authorities

35 U.S.C. § 112 10

Ambion, *The Basics*: *RNase Control*, Fig. 2 (2006), at
http://www.ambion.com/techlib/basics/rnasecontro 6

Webster's Third New International Dictionary (1993) 12, 21, 28

American Heritage Collegiate Dictionary (3d ed. 1993) 13, 19, 21

Merriam Webster's Collegiate Dictionary (10th ed. 1993) ..... *passim*

McGraw-Hill Dictionary of Scientific and Technical Terms (4th ed. 1989) 13, 16

Grant & Hackh's Chemical Dictionary 206 (5th ed. 1987) 16

The Penguin Dictionary of Chemistry 154 (2d ed. 1990) 16

Oxford Dictionary of Biochemical and Molecular Biolog (rev. ed. 2000) 15

Yan Xu, "Tutorial: Capillary Electrophoresis,"
The Chemical Educator, Vol. 1, No. 2, 2, (1996) 3

INTRODUCTION

This brief addresses disputed claim language in U.S. Patent No. 5,385,654 (the "'654 patent"), asserted by Thermo Finnigan LLC ("Thermo") against Applera Corporation ("Applera"). The '654 patent concerns the field of capillary electrophoresis.

I. Technological Background

A. Introduction to Capillary Electrophoresis

Capillary electrophoresis is a technique that is used to separate, detect and analyze ions, *i.e.*, particles that have a net positive or negative electrical charge. Capillary electrophoresis is a fundamental analytical technique used in a wide variety of applications. For example, capillary electrophoresis can be used to detect the presence of impurities in water. Capillary electrophoresis also played a significant role in sequencing DNA for the Human Genome Project.

1. Electric Fields, Ions, and Ion Movement

The electrical charge of an ion permits its movement to be controlled by an electric field. Since opposite charges attract, a negatively charged ion, or anion, will be attracted toward the positive end of an electric field. Similarly, a positively charged ion, or cation, will be attracted toward the negative end of an electric field. If the ions are in a medium that permits them to move (*e.g.*, such as a fluid or a gel), the attractive forces caused by an electric field will result in movement, or migration, of the ions.

The speed at which an ion moves under such conditions depends on a variety of factors such as the ion's charge, size, and shape. Generally, the force applied to an ion by an electric field is proportional to the ion's charge. Therefore, other things being equal, increasing an ion's charge will increase the speed of that ion's movement. However, an ion's speed is also influenced by friction between the ion and the supporting medium

(*e.g.*, fluid or gel), which is influenced by the ion's size and shape. For ions of like charge, frictional forces tend to slow down larger ions to a greater extent than smaller ions, so that smaller ions tend to move faster than larger ions.

2. Ion Movement in a Capillary

In capillary electrophoresis, numbers of different ions mixed together are suspended in a fluid known as a "buffer" or a "carrier electrolyte." An electric field then forces the ions of interest to migrate through a capillary (a tube with a very small internal diameter) from one end to the other. Although the ions are introduced at one end of the capillary at the same time, the factors that affect the ions' movement (such as charge, size, and shape) cause the ions to exit the capillary sequentially at the other end. That is, the forces that affect the ions' movement as they pass through the capillary will cause the ions, which were initially all mixed together, to *separate* into distinct groups.

As an example, if a sample solution contained two different types of ions, the first ions to exit the capillary would be the faster moving (*e.g.*, smaller and more highly charged) ions. Ideally, all ions of this first type would exit in a single group, and then at a later time all ions of the second type (*e.g.*, larger and lesser charged) would exit as a second distinct group. Generally, the sample solution will contain many different types of ions and, ideally, the capillary electrophoresis system will be tuned so that each type of ion exits the capillary in its own distinct group, separate from all the other groups.

Separating ions into distinct groups can be useful in a variety of contexts. By concentrating all ions of a single type into a small region, it is possible to detect and analyze even small amounts of a compound. This is useful, for example, when analyzing water for very low levels of toxic impurities such as lead, arsenic, or toxic organic compounds. In addition, capillary electrophoresis provides a means for the separation of

complex mixtures. For example, capillary electrophoresis is capable of separating and detecting the many anions commonly found in explosives and explosives residue.

A basic capillary electrophoresis instrumental set-up (for detection of cations) is shown schematically in Figure 1 below[1]:

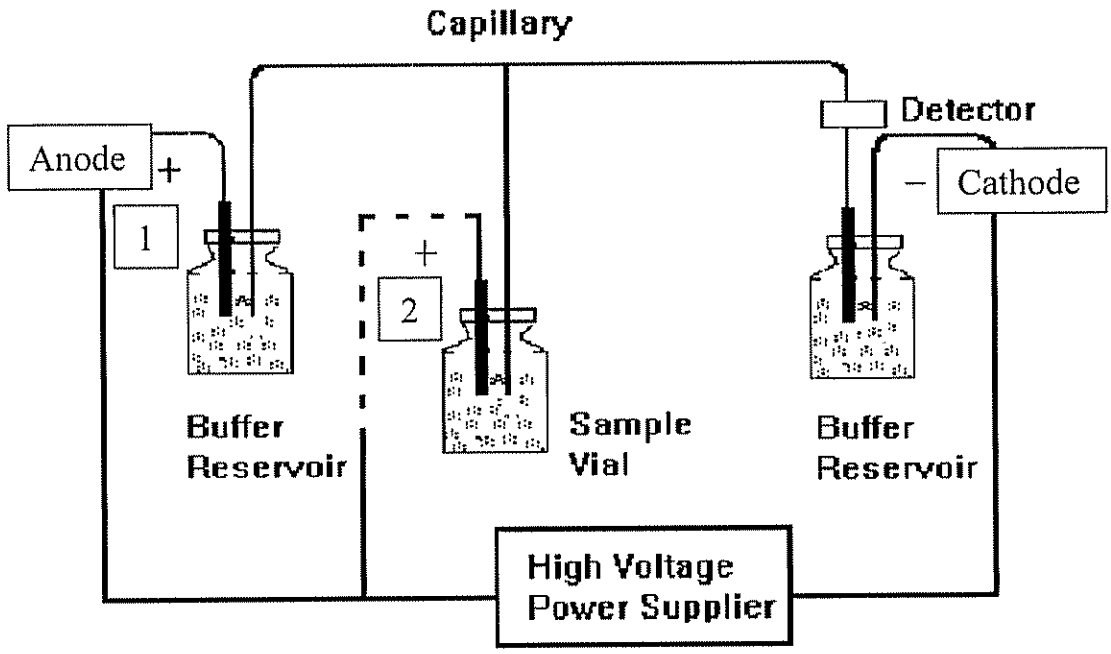

Figure 1. An instrumental set-up of a capillary electrophoresis system that uses voltage to introduce a sample.

The instrument includes: (1) a high-voltage power supply, (2) a narrow diameter capillary, which is typically made of silica (SiO_2), and (3) a detector. The power supply's positive electrode (the "anode") and one end of the capillary are immersed in a reservoir of buffer solution. Similarly, the power supply's negative electrode (the "cathode") and the other end of the capillary are immersed in a second reservoir of the buffer solution.

---

[1] Figure 1 is taken from Yan Xu, "Tutorial: Capillary Electrophoresis," *The Chemical Educator*, Vol. 1, No. 2, 2 (1996). (TA 2.) Citations to "TA" refer to the Appendix filed herewith by Thermo. The numbers "1" and "2" and the words "Anode" and "Cathode" have been added for ease of reference.

One end of the capillary (*e.g.*, the anode end as shown in Figure 1) can be moved between the buffer reservoir position (position "1") and a vial containing the sample to be analyzed (position "2").

During operation, the buffer solution is first loaded into the capillary. The buffer solution is electrically conductive and serves at least two functions. First, the buffer's conductivity allows the voltages generated by the power supply to create an electric field that extends through the capillary (*e.g.*, to complete the electrical circuit). Second, the buffer solution is the fluid medium in which the ions will travel and separate into distinct groups. The capillary may also contain other components, such as a polymer gel or other additives that modify the separation properties of the ions of interest. The polymer gel forms pores through which the ions migrate as they separate into distinct groups. The polymer gel assists ion separation because the larger ions are hindered to a greater extent by the gel and move more slowly than smaller ions through the polymer network.

Once the capillary has been filled with buffer solution, a small amount of the sample solution is "injected" into the capillary. This can be done by moving the end of the capillary from the buffer reservoir (position "1") to the sample vial (position "2") and temporarily applying an appropriate voltage to the sample solution as suggested by the dashed line in Figure 1. Alternatively, sample injection can be achieved by briefly applying a high pressure to the capillary end that is immersed in the sample solution. Once a small amount of sample has been introduced into the capillary, conditions (*e.g.*, voltages or pressures) are adjusted so that no more sample solution will be introduced into the capillary and the capillary is returned to the buffer reservoir for the remainder of the run.

After sample injection, the electric field provided by the conductive buffer solution and the power supply causes ions in the sample to migrate toward the oppositely charged exit end of the capillary, and to separate into groups as they do so. A detector is located so that the ion groups flow through the detector as they migrate toward the capillary exit.[2] The detector generates an output graph, called an "electropherogram," which indicates the ion concentration (*e.g.*, the amount of ions in each group) and the time at which each group passes through the detector.

3. Ion Detection

The detector measures the presence and/or the amount of ions in the capillary. Typically, the detector is part of the capillary tube and the ions pass through the detector as they exit the capillary. A simple illustration of a detector is shown in Figure 2.

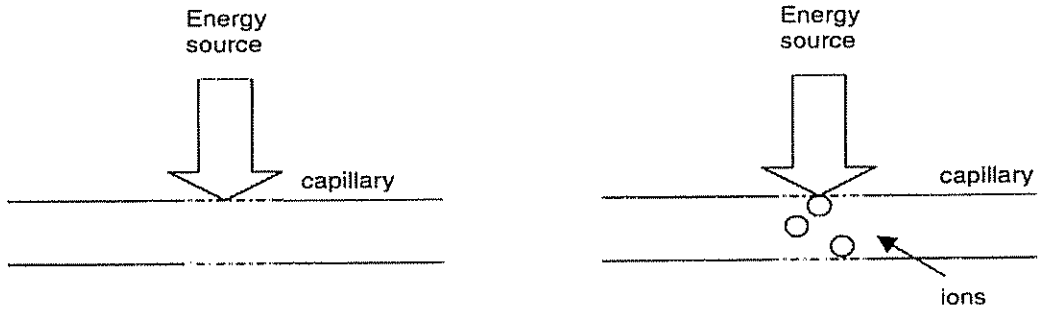

Figure 2

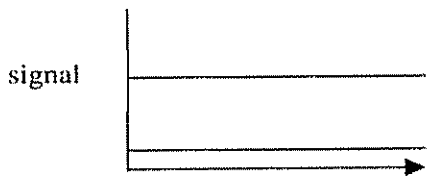

Figure 2a

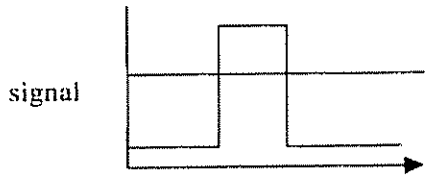

Figure 2b

[2] In Figure 1, the detector is placed near the cathode. Alternatively, the detector could be placed near the anode.

A detector directs electromagnetic radiation, or energy, such as visible or ultraviolet light, through a transparent section or "window" of the capillary. When there is no sample in the detector window, a baseline response is recorded in the electropherogram, as shown in Figure 2a. When sample ions enter the detector window, the electropherogram signal changes in a characteristic way to indicate the presence of sample ions, as shown in Figure 2b.

In "direct detection" methods, the detector monitors a characteristic of the *sample ions* and detects the presence of sample ions directly. In "indirect detection" methods, the detector monitors a characteristic of the *buffer* and indirectly detects the presence of sample ions through changes in the buffer characteristic.

In some detection methods, a specific wavelength of light energy is used because the sample ions behave in a characteristic way with that particular wavelength of light. For example, the sample ions may selectively absorb or emit one wavelength of light, but not another. The detector observes changes to that selective wavelength of light due to its absorbance or emission (*i.e.*, fluorescence) by the sample ions to generate the electropherogram.

A typical detector that monitors the fluorescence of a particular wavelength of light produces an electropherogram as shown in Figure 3 below.[3]

---

[3] Ambion, *The Basics: RNase Control*, Fig. 2 (2006), at http://www.ambion.com/techlib/basics/rnasecontrol.

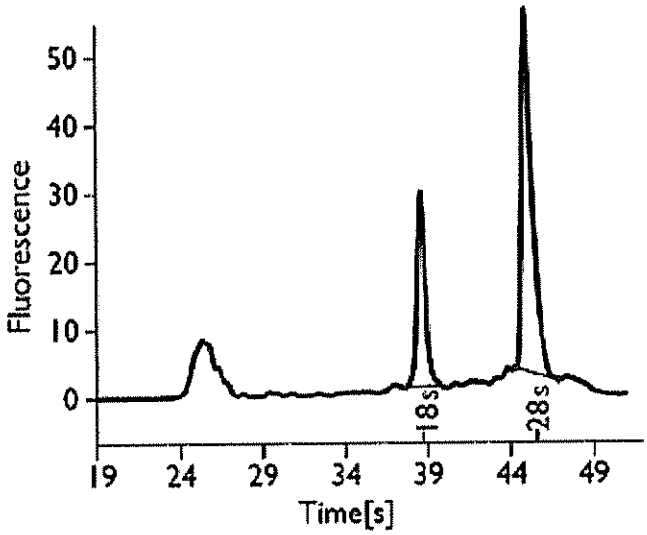

Figure 3. An electropherogram.

B. Electroosmotic Flow

Another concept relevant to capillary electrophoresis is electroosmotic flow. During capillary electrophoresis, the electric field affects more than just the sample ions; ions of the buffer solution also migrate under the influence of the electric field. Also, as the ions move from one end of the capillary to the other, they tend to drag some of the buffer solution with them. This fluid transport generally results in a flow of fluid called "electroosmotic flow." Electroosmotic flow can significantly reduce or increase the time it takes an ion to reach the detector.

In Figure 1, for example, buffer cations can migrate towards the cathode, resulting in an electroosmotic flow towards the cathode end of the capillary. In the example illustrated in Figure 1, sample cations of interest will also migrate toward the cathode in the direction of the flow, so that the effects of electric-field induced migration and electroosmotic flow are additive to one another. The sample cations may be thought of as "fish swimming downstream" toward the exit end of the capillary (and the detector). In this case, the sample ions will have less time to separate into groups before reaching the

detector. Conversely, in Figure 1, sample anions are attracted to the positive electrode ("anode") and may migrate in a direction opposite that of the electroosmotic flow. The sample anions may be thought of as "fish swimming upstream" so that the effects of anion migration and electroosmotic flow tend to cancel each other out. If the electroosmotic flow is greater than the sample anion electric-field induced migration, then the net movement of the anion is actually *backwards* -- slowly toward the cathode. On the other hand, if the electric-field induced anion migration is greater than the electroosmotic flow, then the net movement of the anion is (slowly) toward the anode.

Because the electroosmotic flow can affect the performance of a capillary electrophoresis system, it is useful to be able to control, or modify, this flow. For example, an "electroosmotic flow modifier" may be added to the capillary to change the direction or speed of the electroosmotic flow.

C. Effect of Temperature on Separation

Another concept relevant to capillary electrophoresis is temperature. A change in temperature will alter the viscosity of a buffer. The viscosity of the buffer is a factor affecting the electroosmotic flow. Therefore, it may be important to regulate the temperature of the capillary electrophoresis system to ensure consistent separations. Modern instruments typically achieve this by inserting the capillaries into a cartridge and by forcing temperature-controlled air or liquid through the cartridge.

II. The '654 Patent

A. The Invention

The '654 patent describes an improved method for detecting and separating anions in a sample using capillary electrophoresis. Key to the claimed method is the

combination of using a defined temperature control of the capillary while simultaneously monitoring the sample at two different wavelengths of electromagnetic radiation.

The use of precise temperature control of the capillary improves the selectivity of the capillary electrophoresis process by controlling the speed and order in which the anions migrate through the capillary. Because temperature influences the viscosity of the carrier electrolyte in which the sample ions migrate, the feature of precise temperature control further provides a high degree of repeatability for the detection of anions in a sample. (JA 12-14, '654 patent, 2:26-35, 3:21-40, 6:6-8, 6:17-25.)[4]

The feature of simultaneously monitoring the sample at two different wavelengths also enhances the selectivity of the capillary electrophoresis process. By detecting anions in a sample at two different wavelengths at the same time, the capillary electrophoresis method described in the '654 patent collects additional information regarding the anions in the sample. This additional information allows for improved detection and identification of anions in a sample. (JA 13-14, 1-6, '654 patent, 3:41-53, 6:26-42, figs. 1A-1E.)

Asserted claim 11 of the '654 patent is directed to a capillary electrophoresis method for detecting and separating anions in a sample. The claimed method incorporates the features of defined temperature control and simultaneous monitoring of the sample at two different wavelengths. Claim 11 reads as follows:

> A method for detecting and separating anions in a sample using capillary electrophoresis comprising the steps of, providing a capillary filled with a carrier electrolyte, heating or cooling said capillary to a target temperature in the range of from 20° to 60° C., introducing a sample containing one or more anions into said capillary, applying

[4] Citations to "JA" refer to the Joint Appendix filed by the parties.

> an electrical current to said capillary under conditions causing anions in said sample to migrate and separate, and detecting said anions by simultaneously monitoring said sample at two different wavelengths while maintaining the temperature in said capillary to with ±0.5° C. of said target temperature.

(JA 16, '654 patent, 9:35-10:2.)

Asserted claim 15 depends from claim 11 and adds the step of "including an electroosmotic flow modifier in [the] carrier electrolyte." (JA 16, '654 patent, 10:12-14.)

B. The Prosecution History

The application that led to the '654 patent was filed on July 7, 1993. In an initial office action, the examiner rejected certain claims as indefinite under 35 U.S.C. § 112, ¶ 2, or as anticipated by Morin, et al., "Separation of Arsenic Anions by Capillary Zone Electrophoresis with UV Detection" (the "Morin article"). (JA 58, Examiner's Action at 2 (Oct. 20, 1993).) The examiner also initially rejected certain claims, including those originally numbered as claims 14 and 17 (claims 11 and 15 in the issued patent), as anticipated by U.S. Patent No. 5,104,506 (the "Jones '506 patent") or as obvious over the Jones patent in view of the Morin article. (JA 58-59, Examiner's Action at 2-3 (Oct. 20, 1993).) The applicant responded to the initial office action by amending certain claims (original claim 14 was broadened in two respects) and by providing remarks regarding the teachings of the Morin article and the Jones '506 patent. (JA 119, 120-23, Amendment at 3, 4-7 (Jan. 21, 1994).)

In a final office action, the examiner again rejected certain claims as obvious over the Jones '506 patent in view of the Morin article. (JA 128, Examiner's Action at 2 (May 6, 1994).) However, the examiner indicated that other claims, including original claim 14, were allowable over the prior art. (JA 129, Examiner's Action at 3 (May 6, 1994).)

In response to the final office action, the applicant amended claim 1 and indicated its understanding that original claim 14, and all of its dependent claims, were in condition for allowance. (JA 132, Amendment at 2 (July 5, 1994).)

The examiner subsequently issued a Notice of Allowability. The examiner's statement of reasons for allowance indicated that a prior art search failed to reveal any references teaching or suggesting the claimed methods, with particular emphasis on the limitation of "simultaneously monitoring said sample at two different wavelengths while maintaining the temperature in said capillary to within ±0.5°C of said target [temperature]." (JA 134, 136, Notice of Allowability at 2, 4 (July 14, 1994).) As noted, original claims 14 and 17 issued as asserted claims 11 and 15, respectively, in the '654 patent.

III. Basic Principles of Claim Construction

The Federal Circuit recently reaffirmed the basic principles of claim construction in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005) (*en banc*). Briefly stated, those principles are as follows: The words of a claim are to be given the ordinary and customary meaning that a person of ordinary skill in the art would have understood the claim language to have in light of the patent documents at the time the patent application was filed. *See id.* at 1313. A court should derive this "ordinary and customary meaning" by looking to the claim language, the specification, and the prosecution history. *See id.* at 1314-17. In conjunction with this intrinsic evidence, a court may also consider extrinsic evidence—such as dictionaries—although such evidence is generally "less significant" than the intrinsic record in determining the meaning of claim language. *See id.* at 1317, 1318.

IV. Disputed Claim Terms for the '654 Patent

The asserted claims of the '654 patent describe the steps of the inventive capillary electrophoresis method using language that was well understood in the art. Nonetheless, Applera repeatedly seeks to narrow the plain and ordinary meaning of the claim language by importing limitations both from the specification and from references cited during the prosecution history (some of which do not even use the claim terms at issue). In so doing, Applera not only fails to give meaning to the disputed claim terms but actually *changes* the meaning of the claim language.

A. "Anions"[5]

'654 Term	Claim	Thermo Proposal	Applera Proposal
Anions	11	Negatively charged ions.	Low molecular weight monomeric negatively charged ions

Claim 11 of the '654 patent claims a method for detecting and separating "anions" (without qualification) in a sample. (JA 16, '736 patent, 9:35.) The parties' dispute over the term "anions" is whether the claim term includes all "anions," as that word is commonly understood in the art, or whether the claim term is limited to a particular narrow subset of anions as Applera suggests.

In both its plain meaning and its usage throughout the intrinsic record, the term "anions" just means "negatively charged ions." There can be no dispute that the plain and ordinary meaning of the word "anions" -- as anyone who has taken a high school chemistry class would know -- is simply "negatively charged ions." (TA 5, *Webster's Third New International Dictionary* 86 (1993) (defining "anion" to mean "a negatively

---

[5] The proposed constructions are taken from the Parties' Amended Joint Claim Construction Chart (D.I. 54) filed on January 19, 2006.

charged ion"); TA 9, *American Heritage Collegiate Dictionary* 54 (3d ed. 1993) (defining "anion" to mean "[a] negatively charged ion, esp. the ion that migrates to an anode in electrolysis"); TA 16, *Merriam Webster's Collegiate Dictionary* 46 (10th ed. 1993) (defining "anion" to mean "a negatively charged ion"); TA 23, *McGraw-Hill Dictionary of Scientific and Technical Terms* 94 (4th ed. 1989) (defining "anion" to mean "[a]n ion that is negatively charged").) Interpretation of the word "anions" as used in claim 11 should thus involve "little more than the application of the widely accepted meaning of [the] commonly understood word[]." *Phillips*, 415 F.3d at 1314 (noting the helpfulness of general purpose dictionaries in this situation).

Applera's proposed construction, however, seeks to narrow the term "anions" from its plain and ordinary meaning to a particular subset of anions -- namely, only those anions that have a low molecular weight and are monomeric. The intrinsic record does not support such a narrowing interpretation of the term.

As the claims and the specification indicate, the invention of the '654 patent is directed to improved methods for the detection and separation of anions generally using capillary electrophoresis. (JA 12, '654 patent, 2:23-25.) The specification does not limit the invention to a particular type of anion that is to be detected and separated. On the contrary, it broadly states that the invention "relates to the separation and detection of common anionic species" and that "[b]oth organic and inorganic anions may be separated." (JA 12, '654 patent, 1:1-2, 2:25-26.)

In attempting to narrow the term "anions" from its plain meaning, Applera cites portions of the specification that describe particular embodiments of the invention. For example, the specification describes a preferred embodiment that is "particularly suited to detect such common low molecular weight inorganic and organic anions such as chloride,

nitrate, nitrite, sulfate, and oxalate." (JA 13-14, '654 patent, 3:5-8; 5:44-47.) That preferred embodiment is recited in claim 3, which specifically requires the anions to be "selected from the group consisting of chloride, nitrate, nitrite, sulfate, and oxalate anions." (JA 16, '654 patent, 9:3-6.) In contrast, claim 11 is written more broadly and is not limited to detecting and separating particular types of anions. *See Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1341 (Fed. Cir. 2001) (stating that it is improper to read characteristics of a preferred embodiment into a claim as a limitation). Furthermore, the specification's description of "low molecular weight" anions in a preferred embodiment shows that the inventors knew how to distinguish "low molecular weight" anions from "anions" generally. Thus, the inventors did not intend the word "anions" to mean the same things as "low molecular weight anions." *See Phillips*, 415 F.3d at 1314 (observing that use of the term "steel baffles" strongly implies that the word "baffles" does not necessarily mean objects made of steel).

In support of its proposed construction for the term "anions," Applera also cites to a research disclosure that was cited during prosecution of the '654 patent. That disclosure, however, provides little (if any) insight into how the inventors intended to use the word "anions" in the '654 patent. The cited research disclosure is a one-page summary that describes one very specific capillary electrophoresis application -- "the use of phthalate ion as a carrier electrolyte to separate [nine] anions." (JA 98.) Like the description of the preferred embodiment in the '654 patent, the research disclosure refers

to "low molecular weight anions." Again, this usage suggests that the word "anions" is not synonymous with "low molecular weight anions." *See Phillips*, 415 F.3d at 1314.[6]

Applera also argues that the term "anions" includes the characteristic that the negatively charged ions are "monomeric." A "monomeric unit" is "a group of atoms, derived from a molecule of a given monomer, that comprises any one species of constitutional unit of a polymer" (TA 27 *Oxford Dictionary of Biochemical and Molecular Biolog,* 428 (rev. ed. 2000). A "monomeric" anion, therefore, is capable of combining to form a polymer. However, anions disclosed in the '654 patent, such as chloride, nitrate, nitrite and sulfate are *not* monomers, do not form monomeric units and cannot be incorporated into a polymer as a "constitutional unit of a polymer." Thus, Applera's proposed construction for "anions" would exclude a preferred embodiment of the '654 patent. *See Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1583 (Fed. Cir. 1996) (stating that a construction that does not read on a preferred embodiment is "rarely, if ever, correct").

Furthermore, nowhere does the '654 patent describe "anions" as "monomeric" or even suggest that the claimed "anions" need to be monomeric. On the contrary, the intrinsic evidence demonstrates that the inventors were aware of capillary electrophoresis techniques used to detect and separate polymeric ions. Specifically, the Kurosu article cited in the prosecution history teaches that temperature-controlled capillary

---

[6] In contrast, U.S. Patent No. 5,066,382 (the "Weinberger patent"), which was also cited during prosecution of the '654 patent, expressly defines the word "anions" as "negatively charged molecules." (JA 204, '382 patent, 1:46.)

electrophoresis techniques may be used to separate polymeric ions. (JA 72, Kurosu at 201 (describing the detection and separation of peptides).)

B. "Capillary Electrophoresis"

'654 Term	Claim	Thermo Proposal	Applera Proposal
capillary electrophoresis	11	Electrophoresis, or the movement of ions under the influence of an electric field, that takes place in a capillary tube.	A chemistry technique which utilizes the difference in solute electrophoretic velocity to isolate the various components of a sample in a capillary.

Claim 11 recites a method for detecting and separating anions in a sample using "capillary electrophoresis." Thermo proposes a construction for the term "capillary electrophoresis" -- the movement of ions under the influence of an electric field that takes place in a capillary tube -- that is consistent with its plain meaning. (TA 18, *Merriam Webster's Collegiate Dictionary* 372 (10th ed. 1993) (defining "electrophoresis" as "the movement of suspended particles through a fluid or gel under the action of an electromotive force applied to electrodes in contact with the suspension"); TA 24, *McGraw-Hill Dictionary of Scientific and Technical Terms* 630 (4th ed. 1989) (defining "electrophoresis" as "an electrochemical process in which colloidal particles or macromolecules with a net electric charge migrate in a solution under the influence of an electric current"); TA 31, *Grant & Hackh's Chemical Dictionary* 206 (5th ed. 1987) (defining "electrophoresis" as "[t]he migration of suspended particles in an electric field; [i]n particular, the accelerated chromatographic separation of compounds by immersing each end of the medium in an electrolyte and applying an electric potential"); TA 34, *The Penguin Dictionary of Chemistry* 154 (2d ed. 1990) (defining "electrophoresis" as "[t]he migration of charged particles, colloidal particles or ions through a solution under an

electric field . . . used in analysis, particularly in biochemical applications . . . for both identification and separation").)

This plain meaning of the term is consistent with the specification of the '654 patent. The specification states that "[t]he separation and/or detection of ionic species in chemical analysis is generally carried out using the electrochemical properties of the analytes." (JA 12, '654 patent, 1:13-15.) It then explains that, in capillary electrophoresis, these electrochemical properties include ionic mobility -- in other words, the movement of ions under the influence of an electrical field. (JA 12, '654 patent, 1:15-18.) The specification further elaborates that the rate at which the ions in a sample move from one electrode toward the other in a capillary column may depend on, among other factors, electrical charge, molecular size, ion mobility, and electric field strength. (JA 12, '654 patent, 1:33-37.)

Applera's proposed construction for the term "capillary electrophoresis" -- a "chemistry technique which utilizes the difference in solute electrophoretic velocity to isolate the various components of a sample in a capillary" -- itself requires construction (such as the meaning of "electrophoretic velocity"). Applera's definition is taken from U.S. Patent No. 5,066,382 (the "Weinberger patent"), which was cited during prosecution of the '654 patent. Although the '654 patent incorporates the Weinberger patent by reference to describe the operation of a preferred embodiment, it does so solely for its disclosure of the operation of a thermal control for a particular capillary electrophoresis instrument, not for its background description of capillary electrophoresis in the prior art. (JA 14, '654 patent, 5:1-14.) The Weinberger patent's general discussion of capillary electrophoresis should therefore not be read to define or change the meaning of the term "capillary electrophoresis" as it is used in the '654 patent. *See Schwarz Pharma, Inc. v.*

Warner-Lambert, Co., 95 Fed. Appx. 994, 996, 998 (Fed. Cir. 2004) (unpublished) (holding that patent-in-suit's incorporation by reference of earlier patents was for earlier patents' disclosure of ACE inhibitor compounds, not for their distinction between "carbonate" and "bicarbonate," and, thus, earlier patents were not instructive for construction of "carbonate" in patent-in-suit); *Masimo Corp. v. Mallinckrodt Inc.*, 18 Fed. Appx. 852, 855 (Fed. Cir. 2001) (unpublished) (holding that texts incorporated by reference for the sole purpose of explaining two algorithms that may be used in adaptive filters, and not for the purpose of disclosing alternative types of adaptive filters, did not provide support for interpreting the claim term "adaptive filter").[7] This is especially true when, as in this instance, the specification of the patent that is being construed provides an adequate description of the disputed term.

C. "Carrier Electrolyte"

'654 Term	Claim	Thermo Proposal	Applera Proposal
carrier electrolyte	11, 15	An electrically conductive fluid medium that carries or transports ions	Any electrically conductive fluid medium.

Two limitations in the asserted claims refer to a "carrier electrolyte." The method recited in claim 11 includes the step of "providing a capillary filled with a carrier electrolyte." Dependent claim 15 includes the additional step of "including an electroosmotic flow modifier in said carrier electrolyte."

The specification of the '654 patent defines the term "carrier electrolyte" in accordance with its plain meaning. The specification states: "By 'carrier electrolyte' or

---

[7] *Schwarz Pharma* and *Masimo* are unpublished and may not be cited as precedent. However, they are precisely on point to the issue here and are illustrative, if not precedential.

'buffer,' we mean any electrically conductive fluid medium for the sample." (JA 12, '654 patent, 2:56-57; *see also id.* at 1:25-27.) Thermo's proposed construction seeks to explain the specification's definition in lay terms, by clarifying what a "medium for the sample" is in the context of the '654 patent -- namely, a substance that carries or transports ions. (*See* TA 11, *American Heritage Collegiate Dictionary* 846 (3d ed. 1993) (defining "medium" as "[a]n intervening substance through which something else is transmitted or carried on").) Applera's construction may define an "electrolyte," but does not give meaning to a "carrier electrolyte."

D. "Target Temperature"

'654 Term	Claim	Thermo Proposal	Applera Proposal
target temperature	11	A selected temperature.	A preselected temperature of the fluid in the capillary prior to introducing the sample into the capillary and applying an electrical current to the capillary.

The method recited in claim 11 includes the steps of "heating or cooling said capillary to a target temperature in the range of from 20°C to 60°C." and "maintaining the temperature in said capillary to within ±0.5° C. of said target temperature." As is evident from the plain meaning of the claim language, the "target temperature" is simply a selected temperature. (*See* TA 13, *American Heritage Collegiate Dictionary* 1387 (3d ed. 1993) (defining "target" to mean "[a] desired goal"); TA 20, *Merriam Webster's Collegiate Dictionary* 1206 (10th ed. 1993) (defining "target" to mean "a goal to be achieved").)

The specification of the '654 patent is consistent. In fact, the specification expressly refers to the "target temperature" as a "selected temperature." It states: "A preferred target temperature is in the range of from about 25° to 60° C. At *a selected*

temperature within that range, the speed and order of migration, and thus the selectivity of the separation of the anions may be precisely controlled." (JA 13, '654 patent, 3:28-32 (emphasis added).) The specification later describes the effect of the "selected" target temperature: "Depending upon *the target temperature selected*, the elution order of the anions may be changed." (JA 14, '654 patent, 6:14-16 (emphasis added); *see also* JA 13, '654 patent, 3:21 (referring to "proper selection of a target temperature").)

Despite the plain meaning of the claim language, Applera's proposed construction seeks to impose two additional restrictions on the term "target temperature." First, Applera's proposed construction defines the "target temperature" as a temperature "of the fluid in the capillary." This interpretation contradicts the claim language, which refers only to "heating or cooling *said capillary* to a target temperature" and "maintaining the temperature *in said capillary* to within ±0.5° C. of said target temperature," not to the "fluid in the capillary." (JA 16, '654 patent, 9:35-10:2; *see also* JA 122, Amendment at 6 (Jan. 21, 1994) (referring to heating or cooling "of the capillary").)

Second, Applera's proposed construction defines the "target temperature" to be a "preselected" temperature "prior to introducing the sample into the capillary and applying an electrical current to the capillary." Applera's proposed restriction on *when* the target temperature is selected, however, finds no support in the intrinsic record, let alone the claim language. Although the term "target temperature" first appears in the text of claim 11 prior to the text of "introducing a sample" and "applying an electrical current," it is a well-known principle of claim construction that the steps of a method claim are not ordinarily limited to the order in which they are recited. *See Interactive Gift Express*, 256 F.3d at 1342 ("Unless the steps of a method actually recite an order, the steps are not ordinarily construed to require one."). Moreover, neither the specification nor the

prosecution history imposes any restriction on the target temperature that would require it to be selected prior to introducing a sample into the capillary or applying an electrical current to the capillary. (*See* JA 13, '654 patent, 3:21-40, 6:14-16; JA 121-22, Amendment at 5-6 (Jan. 21, 1994) (stating only that the "target temperature" must fall within the specified range of temperatures).)[8]

E. "Detecting Said Anions by Simultaneously Monitoring Said Sample at Two Different Wavelengths"

'654 Term	Claim	Thermo Proposal	Applera Proposal
Detecting said anions by simultaneously monitoring said sample at two different wavelengths	11	Detecting the anions by monitoring the sample at two different wavelengths at the same time	Detecting the anions in the sample by simultaneously monitoring the absorption of two different wavelengths of light, one of which is not absorbed by the anions.

Claim 11 requires the step of "detecting said anions by simultaneously monitoring [the] sample at two different wavelengths." (JA 16, '654 patent, 9:43-44.) This means that the monitoring of the sample at two different wavelengths occurs at the same time. This is consistent with the plain meaning of the word "simultaneously." (*E g* , TA 12, *American Heritage Collegiate Dictionary* 1271 (3d ed. 1993) (defining "simultaneous" to mean "[h]appening, existing, or done at the same time"); TA 19, *Merriam Webster's Collegiate Dictionary* 1094 (10th ed. 1993) (defining "simultaneous" to mean "existing or occurring at the same time").)

---

[8] In the joint claim construction chart, Applera cites the Morin article in support of its proposed construction for "target temperature." The Morin article, however, does not even use the term "target temperature," let alone suggest a target temperature that must be measured in the fluid of the capillary or selected prior to introducing a sample into the capillary or applying an electrical current. (*See* JA 70, Morin at 362.)

Thermo's construction is also consistent with the specification, which provides examples of simultaneous monitoring of the sample. For instance, the specification describes an embodiment of the invention in which "anions in a sample may be detected by simultaneously monitoring the sample at two different wavelengths with [a] photodetector." (JA 13, '654 patent, 3:41-43.) In another example, the specification describes using a "UV/VIS scanning detector . . . to monitor at 210 nm and 254 nm, simultaneously." (JA 15, '654 patent, 7:24-26.) Figures 1A-1E of the patent illustrate the simultaneous detection data from this latter example, as can be seen from the two lines present in each electropherogram. (JA 13, 15, 2-6, '654 patent, 4:7-10, 7:27-40, figs. 1A-1E.)[9]

Rather than give meaning to the claim limitation, Applera's proposed construction actually *changes* the meaning of the "simultaneously monitoring" limitation by adding two requirements that do not appear in either the claim language or the specification. First, Applera's proposed construction changes the claim language from "simultaneously monitoring said sample at two different wavelengths" to "simultaneously monitoring the *absorption of* two different wavelengths." Second, Applera's proposed construction adds the requirement that one of the two wavelengths *not* be absorbed by the anions. Neither of these limitations finds support in the intrinsic evidence.

---

[9] The prosecution history further supports Thermo's construction. During prosecution, the applicant distinguished U.S. Patent No. 5,104,506 (the "Jones '506 patent") on the basis that it "do[es] not teach simultaneous monitoring at two wavelengths." (JA 123, Amendment at 7 (Jan. 21, 1994).) The applicant explained that the detection taught by the Jones '506 patent was not simultaneous because it "was carried out at a single wavelength" -- "254 or 272 nm." (JA 123, Amendment at 7 (Jan. 21, 1994) (citing JA 215, '506 patent, 3:34-36).) The applicant further pointed out that "[n]one of the graph figures [in the Jones '506 patent] show simultaneous detection data. . . ." (JA 123, Amendment at 7 (Jan. 21, 1994).)

To begin with, the language of claim 11 broadly refers to "detecting" anions by "monitoring [the] sample." It does not identify a particular characteristic of the sample (such as absorbance) that is to be monitored. In contrast, dependent claim 12 is more specifically directed to an absorbance-monitoring detection method in which the "carrier electrolyte contains a light-absorbing co-anion" and the anions are "detected indirectly using a photometric detector." (JA 16, '654 patent, 10:3-6.) The contrast in claim language between claims 11 and 12 thus shows that the patentee chose not to limit the "simultaneously monitoring" step of claim 11 to monitoring absorption, let alone monitoring absorption at one wavelength that is not absorbed by the anions. *See Phillips*, 415 F.3d at 1314-15 (stating that differences among claims can be a useful guide in understanding the meaning of particular claim terms).

The specification's description of the claimed detection step is also not as narrow as Applera's proposed construction would require. The specification broadly explains that "[d]etection of the anions may be by direct or indirect techniques." (JA 12, '654 patent, 2:48-51.) The specification also makes clear that an absorbance-measuring detector is only one type of detector that can be used in the claimed method. It states: "A detector is placed downstream from the position where the sample is introduced into the capillary, and an electric current is applied to cause the ions in the sample to migrate past the detector. A *preferred* detector is one which utilizes UV/visible absorbance such as a multiwavelength, scanning UV/VIS detector." (JA 13, '654 patent, 4:62-68 (emphasis added).) It would be improper to restrict the "simultaneously monitoring" limitation of claim 11 to a particular type of detection, especially when the specification makes clear that other detectors may be used and that an absorbance-monitoring detector is used only

in a preferred embodiment. (*See* JA 13, '654 patent, 4:41-43 (noting other embodiments in which detection is accomplished using a conductivity detector or mass spectrometer).)

Finally, the references cited during prosecution of the '654 patent illustrate that the inventors were aware of prior art detection methods that monitored wavelength-dependent properties other than absorbance, such as fluorescence. For example, U.S. Patent No. 5,104,506 (the "Jones '506 patent") describes both direct photometric detection and fluorescent detection as examples of "conventional photometric means" for detecting ions using capillary electrophoresis. (JA 214, '506 patent, 1:50-52; *see also id* at 1:59-62 ("Indirect photometric detection has been described using *fluorescent*, ultraviolet (UV) and UV-visible (UV-vis) absorbing ions in the background electrolyte." (emphasis added)).) Similarly, U.S. Patent No. 5,066,382 (the "Weinberger patent") describes a capillary electrophoresis technique in which "solute bands are . . . *detected by monitoring* a bulk property of the buffer such as refractive index, photometric absorbance, [or] fluorescence." (JA 204, '382 patent, 2:14-16 (emphasis added); *see also* JA 208, '382 patent, 9:26-31 ("The monochromator may be generating light of a given bandwidth for the purpose of UV-visible photometric absorbance detection, fluorescence detection, refractive index detection, as well as any other means of photometric detection.").)

F. "Maintaining the Temperature in Said Capillary to Within ±0.5° C. of Said Target Temperature"

'654 Term	Claim	Thermo Proposal	Applera Proposal
maintaining the temperature in said capillary to within ±0.5° C. of said target temperature	11	Maintaining the temperature in the capillary to within ±0.5° C. of the target temperature.	Maintaining the temperature throughout the fluid in the capillary to within ±0.5° C. of the target temperature by monitoring electrical resistance in the capillary and maintaining the resistance at a constant level.

Claim 11 recites the step of "maintaining the temperature in said capillary to within ±0.5° C. of said target temperature." As Thermo's proposed construction demonstrates, the plain meaning of this claim language is clear and requires no interpretation.

Nonetheless, Applera once again seeks to alter the language of claim 11 by inserting two additional limitations into the claim. First, Applera's proposed construction adds the words "throughout the fluid" to describe where the temperature must be maintained. As discussed above in conjunction with the "target temperature" limitation, Applera's construction contradicts the claim language, which refers to "maintaining the temperature *in said capillary*," not to any "fluid." (JA 16, '654 patent, 10:1-2 (emphasis added); *see also id.* at 9:38-39 (reciting "heating or cooling *said capillary* to a target temperature" (emphasis added)).) The specification of the '654 patent distinguishes between maintaining the temperature in the capillary (as the claim states) and to maintaining the temperature of the fluid in the capillary. (*E.g.*, JA 13, '654 patent, 3:23-25.) Further, even as to the temperature of the fluid, nothing in the intrinsic evidence suggests that the temperature would have to be maintained at all points *throughout* the fluid (as compared to *in* the fluid).

Second, Applera's proposed construction tacks on the words "by monitoring electrical resistance in the capillary and maintaining the resistance at a constant level" to the end of the "maintaining the temperature" limitation. Clearly, the claim language provides no basis for this restriction, as it refers to "maintaining the temperature" in the capillary rather than "maintaining the resistance" in the capillary, and indeed never refers to resistance at all. Nor does the specification of the '654 patent limit the method by which the temperature in the capillary must be maintained to a particular technique of "monitoring electrical resistance." On the contrary, the specification teaches generally the benefit of precise temperature control regardless of the method employed, noting that temperature control benefits both the reproducibility of the process as well as the selectivity of the anion separation. (JA 13, '654 patent, 3:38-40; JA 13, *id.* at 3:65-4:1; JA 14, *id.* at 6:17-21.) The specification discloses a way of maintaining the temperature that does not involve monitoring the electrical resistance. It states that in a preferred embodiment "[t]he temperature of the capillary tube may be controlled by forced air or liquid circulating around the capillary or by placing the capillary between metal radiator plates." (JA 13, '654 patent, 4:59-62.) Limiting the claimed step of "maintaining the temperature in said capillary" to Applera's proposed step of maintaining the electrical resistance in the capillary would apparently exclude this preferred embodiment. *See Vitronics*, 90 F.3d at 1583 (Fed. Cir. 1996) (stating that a construction that does not read on a preferred embodiment is "rarely, if ever, correct").

In support of its proposed claim construction, Applera again cites U.S. Patent No. 5,066,382 (the "Weinberger patent"), which is incorporated by reference into the '654 patent to describe the operation of a preferred embodiment. (JA 14, '654 patent, 5:1-14.) The Weinberger patent does describe a capillary electrophoresis machine that monitors

and maintains the electrical resistance in the capillary at a constant level. (JA 207, 209, '382 patent, 7:63-8:12, 11:28-12:34.) However, it is improper to import this limitation into claim 11 of the '654 patent.

As an initial matter, the Weinberger patent describes maintaining the temperature of the capillary by using a fan and a Peltier device to pump heat into or out of a chamber that houses an air-cooled cartridge. Monitoring the electrical resistance of the capillary is merely a way of determining how much heat must be pumped into or out of the chamber; it is not the means by which the temperature of the capillary is actually maintained. (*See* JA 209, '382 patent, 12:25-34.) Moreover, the specification of the '654 patent explains that the Weinberger patent describes the operation of thermal control in a particular capillary electrophoresis instrument, which is used only in a preferred embodiment of the '654 patent. (JA 14, '654 patent, 5:1-14.) Regardless of what the Weinberger patent discloses, the specification of the '654 patent makes clear that the invention of the '654 patent is not limited to the use of such an instrument. (JA 14, '654 patent, 5:1, 5:10-12 (stating that a "preferred embodiment" uses a capillary electrophoresis instrument such as described in the Weinberger patent and that, alternatively, "a manual method may be used").) Again, it would be inappropriate to limit claim 11 to one embodiment described in the specification. *See Phillips*, 415 F.3d at 1320 (stating that importing a limitation from the specification into a claim is "one of the cardinal sins of patent law").

G. "Electroosmotic Flow"

'654 Term	Claim	Thermo Proposal	Applera Proposal
electroosmotic flow	15	Flow in a capillary under the influence of an electric field	The bulk flow of liquid due to the effect of an electric field on cations adjacent to anionic groups immobilized on the capillary wall.

The method recited in claim 15 of the '654 patent includes the step of "including an electroosmotic flow modifier in said carrier electrolyte." Thermo's proposed construction of the term "electroosmotic flow" is that term's plain meaning – "flow in a capillary under the influence of an electric field." (TA 18, *Merriam Webster's Collegiate Dictionary* 372 (10th ed. 1993) (defining "electroosmosis" as "the movement of a liquid out of or through a porous material or a biological membrane under the influence of an electric field"); TA 6, *Webster's Third New International Dictionary* 733 (1993) (defining "electroosmosis" as "the movement of a conducting liquid (as water in clay) through a porous diaphragm under the action of an electromotive force applied to electrodes on opposite sides of the diaphragm").)

Applera's proposed construction for the term "electroosmotic flow" is apparently again derived from the specification of the prior art Weinberger patent. (JA 210, '382 patent, 13:50-14:64.) As discussed above in connection with the claim term "capillary electrophoresis," the '654 patent incorporates the Weinberger patent by reference only for its disclosure of the operation of a thermal control for a particular capillary electrophoresis instrument. It does not incorporate the Weinberger patent by reference for its prior art description relating to electroosmotic flow. (JA 14, '654 patent, 5:1-14.) It certainly never says that the Weinberger patent somehow defines the claim terms of the '654 patent.

In any event, Applera's proposed construction cannot be correct because it is inconsistent with the specification of the '654 patent. Applera's construction imposes a limitation on the direction of the "electroosmotic flow" by defining the flow in terms of the effect of an electric field on "cations adjacent to anionic groups immobilized on the capillary wall." The polarity required by Applera's construction would result in electroosmotic flow in only one direction -- from anode to cathode. The specification of the '654 patent, however, contemplates that the direction of the electroosmotic flow may be reversed. (JA 12, 14, 15, '654 patent, 2:63-67, 5:33-37, 6:47-54, 8:35-36.) In other words, the electroosmotic flow may move from anode to cathode or from cathode to anode. Therefore, an interpretation of the term "electroosmotic flow" that is consistent with that term's usage in the specification cannot be limited to a particular polarity. For this reason, Applera's proposed construction, which restricts the "electroosmotic flow" to movement in one particular direction by its arrangement of cations and anionic groups, cannot be correct.

H. "Electroosmotic Flow Modifier"

'654 Term	Claim	Thermo Proposal	Applera Proposal
electroosmotic flow modifier	15	Substance that modifies the electroosmotic flow.	A small cationic molecule that neutralizes the charge on the capillary wall

The specification of the '654 patent explains generally that electroosmotic flow modifiers can be used to improve sensitivities for the detection of certain ions. (JA 12, '654 patent, 2:11-15.) Throughout its disclosure, the specification consistently describes "electroosmotic flow modifiers" as controlling the speed and/or direction of the electroosmotic flow. (JA 12, '654 patent, 2:63-67.) The specification further states that "there are many electroosmotic flow modifiers known in the art" and identifies some

electroosmotic flow modifiers as preferred for use in the claimed invention. (JA 12-13, 14, '654 patent, 2:67-3:4, 5:33-43.)

Applera's proposed construction once again seeks to impose limitations not in the claim, first of a particular polarity -- *i.e.*, that the electroosmotic flow modifier be a "cationic" molecule, and second that the flow modifier must operate in a particular way, *i.e.*, by "neutralizing the charge in the capillary wall." Limiting the claimed "electroosmotic flow modifier" to a cationic molecule would only allow the flow to be modified in one direction, which is contrary to the plain meaning and specification. The specification of the '654 patent twice refers broadly to the "many electroosmotic flow modifiers known in the art." (JA 12, 14, '654 patent, 2:67-68, 5:37-38.) Such electroosmotic flow modifiers were not limited to cationic molecules and included, for example, neutral molecules, and did not always "neutralize[] the charge in the capillary wall."

CONCLUSION

For the foregoing reasons, Thermo respectfully requests that the Court construe the disputed claim terms of the '654 patent in accordance with Thermo's proposed constructions. A proposed Order setting forth Thermo's proposed constructions is being submitted with this brief.

Kelly E. Farnan

Frederick L. Cottrell, III (#2555)
(Cottrell@RLF.com)
Kelly E. Farnan (#4395)
(Farnan@RLF.com)
Richards, Layton & finger
One Rodney Square
920 N. King Street
P.O. Box 551
Wilmington, DE 19899
(302) 651-7700

Attorneys for Thermo Finnigan LLC

Of Counsel:

William L. Lee
Wayne L. Stoner
Richard Goldenberg
Stephen M. Muller
Mary Rose Scozzafava
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109
(617) 526-6000

Dated: January 20, 2006

CERTIFICATE OF SERVICE

I hereby certify that on January 20, 2006, I electronically filed the foregoing document with the Clerk of Court using CM/ECF which will send notification of such filings, and hand delivered, to the following:

Josy W. Ingersoll
Karen L. Pascale
Adam W. Poff
Karen E. Keller
Young, Conaway, Stargatt & Taylor, LLP
The Brandywine Building
1000 West Street, 17th Floor
Wilmington, DE 19899-0391

I hereby certify that on January 20, 2006 I sent the foregoing document by Federal Express, next business day delivery, to the following non-registered participants:

Walter E. Hanley, Jr.
James Galbraith
Huiya Wu
Kenyon & Kenyon
One Broadway
New York, NY 10004

William G. James, II
Fred T. Grasso
Kenyon & Kenyon
1500 K Street N.W., Suite 700
Washington, DC 20036

Kelly E. Farnan

Kelly E. Farnan (#4395)
Farnan@RLF.com